Remarks

Claims 492-545 are presently pending in the subject application.

Reconsideration and allowance are respectfully requested in view of the above amendments and the following remarks.

Claims 442-491 are canceled herein without prejudice to the prosecution of the subject matter of these claims in this or a future continuing application.

Claims 492-545 are new and correspond to previously pending claims in the subject application as indicated in the Claim Chart attached hereto. *See* Attachment A. In particular, new independent claims 492 and 517 recite a base sequence contained within a recited amplification oligonucleotide which includes a cluster of at least four ribonucleotides modified to include a 2'-O-methyl substitution to the ribofuranosyl moiety. As defined in the specification, a "cluster" of four modified ribonucleotides means that four of five consecutive ribonucleotides are modified to include a 2'-O-methyl substitution to the ribofuranosyl moiety. *See, e.g.,* specification at page 13, lines 18-19. New independent claims 505 and 532 recite at least one amplification oligonucleotide having at least one ribonucleotide modified to include a 2'-O-methyl substitution to the ribofuranosyl moiety in combination with a labeled oligonucleotide probe capable of specifically hybridizing to a base sequence contained in an extension product or a transcription product which is generated using the claimed amplification oligonucleotide to form a duplex stable for detection in the presence of non-target nucleic acid in a sample under nucleic acid assay conditions. Support for such a probe can be found in the specification at, for example, page 3, lines 15-20, page 12, lines 21-28, page 13, lines 1-4 and 24-28, and page 19, line 21 *et seq.*

Applicants note with appreciation the Examiner's indication that the provisional double patenting rejection in view of application Serial No. 09/565,427 and the Section 102(e) rejection in view of Gemen *et al.*, U.S. Patent No. 5,679,553, have been withdrawn.

Interview Summary

Applicants wish to thank the Examiner for participating in a telephonic interview conducted on September 5, 2002. During that interview, Applicants focused on the references cited by the Examiner under 35 U.S.C. § 102(b) in the most recent Office Action. Applicants first noted that Ullu *et al.*, *J. Biol. Chem.* (1993) 268(18):13068-13073, concerns an *in vivo* amplification in which exogenous nucleic acid polymerases are not provided to the permeabilized cells to facilitate amplification. Applicants also stressed that Ullu provides no suggestion that the disclosed 2'-O-methyl oligonucleotides might be useful for amplifying a target sequence. Second, Applicants pointed out that Cook *et al.*, U.S. Patent No. 5,914,396, does not disclose amplification oligonucleotides containing the claimed modifications to amplify a target sequence nor does Cook suggest that such modified oligonucleotides might be useful for amplifying a target sequence. *See* Cook at Example 90 in column 38. Additionally, Applicants observed that Cook does not disclose oligonucleotides containing clusters of 2'-O-methyl modified ribonucleotides in combination with a nucleic acid polymerase for performing an amplification. The Examiner agreed and indicated that the claims would likely be allowable if amended to indicate that the claimed amplification oligonucleotides include clusters of 2'-O-methyl modifications.

Applicants also addressed the propriety of the Examiner's restriction requirement with respect to dependent claims further reciting a target capture oligonucleotide. Because the requirement was made final in the Office Action dated April 23, 2002, the Examiner stated that the requirement would have to be maintained with respect to the indicated claims. However, the Examiner agreed not to extend the restriction requirement to newly added dependent claims reciting a target capture oligonucleotide. Support for target capture oligonucleotides which can be directly or indirectly immobilized on a solid support can be found in the specification at, for example, the paragraph bridging pages 18 and 19 and page 25, line 5 *et seq.*

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 459, 464-467 and 481-484 stand rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants submit that these rejections are rendered moot by the cancellation of claims 459, 464-467 and 481-484 herein. Accordingly, withdrawal of these rejections is respectfully requested.

Rejections Under 35 U.S.C. § 102

Claims 458-460, 464-466, 472-477, 481-483 and 489-491 stand rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Ullu *et al.*, *J. Biol. Chem.* (1993) 268(18):13068-13073. Applicants respectfully traverse this rejection for the reasons that follow.

Ullu is cited by the Examiner for disclosing unlabeled RNA oligonucleotide primers comprising 2'-O-methyl modified ribonucleotides which hybridize to a target sequence in the trypanosome splice leader sequence. Ullu is further cited for disclosing the 2'-O-methyl modified oligonucleotides in combination with other reagents for performing an amplification reaction.

Applicants submit that Ullu does not disclose providing 2'-O-methyl modified oligonucleotide primers to amplify a target sequence in the trypanosome splice leader sequence nor does Ullu suggest that the disclosed 2'-O-methyl modified oligonucleotides might be used to amplify a target sequence. Instead, Ullu discloses the use of 2'-O-methyl modified oligonuceotides to mask various regions of the trypanosome spliced leader (SL) RNA to search for functional elements of the SL molecule. Before introducing these 2'-O-methyl modified oligonucleotides into trypanosome cells, the cells are permeabilized and exposed to a transcription mixture which includes nucleotide triphosphates. *See* "Results" section of Ullu at page 13069 and Attachment B, Ullu *et al.*, *Nucleic Acids Res.* (1990) 18(11):3319-3326. Ullu does not disclose a transcription mixture including a polymerase for performing an amplification reaction. This distinction is acknowledged by the Examiner's exclusion of canceled, dependent claims 461 and 462 from this rejection.

While the Examiner's rejection includes claims 464, 481 and their dependents, the Examiner has never explained the relevance of Ullu to this group of claims. Thus, Applicants submit that the Examiner has failed to establish that Ullu discloses an oligonucleotide probe which preferentially hybridizes to a base sequence contained in either an extension or transcription product formed using a 2'-O-methyl modified amplification oligonucleotide over non-target nucleic acid in a sample under nucleic acid assay conditions. Moreover, newly added independent claims 506 and 537 recite a labeled oligonucleotide probe, which is nowhere disclosed or suggested by Ullu, who provides that the synthesized SL RNA is labeled for detection rather than an oligonucleotide which binds to the synthesized SL RNA. *See, e.g.,* "Results" section of Ullu at page 13069 *et seq.*

Claims 458, 461, 462, 472-475, 478-480 and 489-491 stand rejected by the Examiner under 35 U.S.C. § 102(e) as being anticipated by Cook *et al.*, U.S. Patent No. 5,914,396. Applicants respectfully traverse this rejection for the reasons that follow.

Cook is cited by the Examiner for disclosing 2'-O-methyl oligonucleotides which hybridize to a target nucleic acid sequence. Cook is further cited by the Examiner for disclosing the use of these oligonucleotides in an assay in which the target sequence is synthesized using T7 RNA polymerase and nucleotide triphosphates.

Applicants first observe that the Examiner's reasons for this rejection fail to establish that the modified olgonucleotides disclosed by Cook could be used to amplify a target nucleic acid sequence. Notwithstanding, Applicants' newly added claims recite a cluster of 2'-O-methyl modified ribonucleotides, incorporating the limitation of former claims 459 and 476 into the new claims. As noted above, the specification defines a "cluster" to include four of five consecutive ribonucleotides modified to include a 2'-O-methyl substitution. *See, e.g.,* specification at page 13, lines 18-19. During Applicants' interview with the Examiner on September 5, 2002, the Examiner reaffirmed her position that oligonucleotides including clusters of 2'-O-methyl modifications in combination with

a transcribed target sequence are not disclosed by Cook. Applicants also note that the Examiner has excluded kits which further include oligonucleotide probes from this rejection.

For the reasons presented above, Applicants submit that the newly added claims are fully patentable in view of the cited references. Accordingly, withdrawal of these rejections is respectfully requested.

Terminal Disclaimer

Applicants are filing herewith a terminal disclaimer in view of U.S. Patent No. 6,130,038, which issued from parent application Serial No. 08/893,300.

Conclusion

Applicants submit that the subject application is in condition for allowance and Notice to that effect is respectfully requested.

Please charge any fees due in connection with this Reply to Deposit Account 07-0835 in the name of Gen-Probe Incorporated.

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REPLY

Serial No. 09/523,237
Atty. Docket No. GP068-03.CN1

Certificate of Transmission

I hereby certify that this correspondence (and any referred to as attached) is being sent by facsimile to 703-746-5206 on the date indicated below to the Commissioner for Patents, Washington, D.C. 20231.

Respectfully submitted,

Date: September 17, 2002 By: _____

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